SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

Product Identifier

Material Name: Torisel Injection

Trade Name: TORISEL; GD-TEMSIROLIMUS
Synonyms: Temsirolimus Concentrate for Injection; Temsirolimus Concentrate for Infusion
Chemical Family: Not determined

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Antineoplastic

Details of the Supplier of the Safety Data Sheet

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-800-879-3477

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Reproductive Toxicity: Category 1B
Acute aquatic toxicity: Category 1
Chronic aquatic toxicity: Category 1
Flammable liquids- Category 2

Label Elements

Signal Word: Danger
Hazard Statements: H360FD - May damage fertility. May damage the unborn child.
H225 - Highly flammable liquid and vapor
H400 - Very toxic to aquatic life
H410 - Very toxic to aquatic life with long lasting effects

Precautionary Statements:

P201 - Obtain special instructions before use
P202 - Do not handle until all safety precautions have been read and understood
P210 - Keep away from heat/sparks/open flames/hot surfaces. - No smoking
P233 - Keep container tightly closed
P240 - Ground/Bond container and receiving equipment
P241 - Use explosion-proof electrical/ventilating/lighting/equipment
P242 - Use only non-sparking tools
P243 - Take precautionary measures against static discharge
P280 - Wear protective gloves/protective clothing/eye protection/face protection
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P303 + P361 + P353 - IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower
P370 + P378 - In case of fire: Use .? for extinction
P403 + P235 - Store in a well-ventilated place. Keep cool
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations
P273 - Avoid release to the environment
P391 - Collect spillage

Other Hazards

An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

Note:

This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Citric acid, anhydrous	77-92-9	201-069-1	Not Listed	*
Ethanol	64-17-5	200-578-6	Flam. Liq. 2 (H225)	42.7
Temsirolimus	162635-04-3	Not Listed	Repr.1B (H360FD) Aquatic Acute 1 (H400) Aquatic Chronic 1 (H410)	2.7
Propylene glycol	57-55-6	200-338-0	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
DL-Alpha tocopherol	10191-41-0	233-466-0	Not Listed	*

Additional Information: * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.
In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the CLP/GHS abbreviations mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Description of First Aid Measures

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed

Notes to Physician: None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

Fire / Explosion Hazards: Flammable liquid.

Advice for Fire-Fighters

During all firefighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures

Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions

Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up

Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Cleanup operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling

Flammable liquid and vapor- keep away from ignition sources and clean up spills promptly. Eliminate possible ignition sources (e.g., heat, sparks, flame, impact, friction, electricity), and follow appropriate grounding and bonding procedures. Avoid contact with eyes, skin, and clothing. Use appropriate personal protective equipment. Wash thoroughly after handling. Minimize generating airborne mists and vapors. Avoid breathing mist or aerosols. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls. Refer to Section 12 - Ecological Information, for information on potential effects on the environment.

Conditions for Safe Storage, Including any Incompatibilities

Storage Conditions: Store as directed by product packaging.
Specific end use(s): Pharmaceutical drug product

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

Refer to available public information for specific member state Occupational Exposure Limits.

Ethanol

ACGIH Threshold Limit Value (STEL)	1000 ppm
Australia TWA	1000 ppm 1880 mg/m^3
Austria OEL - MAKs	1000 ppm 1900 mg/m^3
Belgium OEL - TWA	1000 ppm 1907 mg/m^3
Bulgaria OEL - TWA	1000 mg/m^3
Czech Republic OEL - TWA	1000 mg/m^3
Denmark OEL - TWA	1000 ppm 1900 mg/m^3
Estonia OEL - TWA	500 ppm 1000 mg/m^3
Finland OEL - TWA	1000 ppm 1900 mg/m^3
France OEL - TWA	1000 ppm 1900 mg/m^3
Germany - TRGS 900 - TWAs	500 ppm 960 mg/m^3
Germany (DFG) - MAK	500 ppm 960 mg/m^3
Greece OEL - TWA	1000 ppm 1900 mg/m^3
Hungary OEL - TWA	1900 mg/m^3
Latvia OEL - TWA	1000 mg/m^3
Lithuania OEL - TWA	500 ppm 1000 mg/m^3
Netherlands OEL - TWA	260 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

OSHA - Final PELS - TWAs:	1000 ppm 1900 mg/m^3
Poland OEL - TWA	1900 mg/m^3
Portugal OEL - TWA	1000 ppm
Romania OEL - TWA	1000 ppm 1900 mg/m^3
Russia OEL - TWA	1000 mg/m^3
Slovakia OEL - TWA	500 ppm 960 mg/m^3
Slovenia OEL - TWA	1000 ppm 1900 mg/m^3
Sweden OEL - TWAs	500 ppm 1000 mg/m^3
Switzerland OEL -TWAs	500 ppm 960 mg/m^3
Vietnam OEL - TWAs	1000 mg/m^3

Propylene glycol

Australia TWA	150 ppm 474 mg/m^3 10 mg/m^3
Ireland OEL - TWAs	150 ppm 470 mg/m^3 10 mg/m^3
Latvia OEL - TWA	7 mg/m^3
Lithuania OEL - TWA	7 mg/m^3

Temsirolimus

Pfizer Occupational Exposure Band (OEB):	OEB 5 (control exposure to <1ug/m^3)

Exposure Controls

Engineering Controls:	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.
Personal Protective Equipment:	Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.
Hands:	Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)
Eyes:	Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)
Skin:	Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)
Respiratory protection:	Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL (e.g. particulate respirator with a full mask, P3 filter). (Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.)

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Liquid	**Color:**	Clear, colorless to pale yellow
Odor:	No data available.	**Odor Threshold:**	No data available.
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

Solvent Solubility: No data available
Water Solubility: No data available
pH: No data available.
Melting/Freezing Point (°C): No data available
Boiling Point (°C): 93
Partition Coefficient: (Method, pH, Endpoint, Value)
Temsirolimus
Measured 6.75 Log P 4.93
Citric acid, anhydrous
No data available
Ethanol
No data available
DL-Alpha tocopherol
No data available
Propylene glycol
No data available
Decomposition Temperature (°C): No data available.

Evaporation Rate (Gram/s): No data available
Vapor Pressure (kPa): No data available
Vapor Density (g/ml): No data available
Relative Density: No data available
Specific Gravity: 0.9237 g/mL
Viscosity: No data available

Flammablity:
- **Autoignition Temperature (Solid) (°C):** No data available
- **Flammability (Solids):** No data available
- **Flash Point (Liquid) (°C):** 21.1
- **Upper Explosive Limits (Liquid) (% by Vol.):** No data available
- **Lower Explosive Limits (Liquid) (% by Vol.):** No data available

10. STABILITY AND REACTIVITY

Reactivity: No data available
Chemical Stability: Stable under normal conditions of use.
Possibility of Hazardous Reactions
- **Oxidizing Properties:** No data available
- **Conditions to Avoid:** Fine particles (such as dust and mists) may fuel fires/explosions.
- **Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers
- **Hazardous Decomposition Products:** No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients.

Short Term: Accidental ingestion may cause effects similar to those seen in clinical use.

Long Term: Chronic ingestion of ethanol has been associated with an increased incidence of cancer, liver cirrhosis, and, if ingested during pregnancy, congenital malformations.

Known Clinical Effects: Adverse effects associated with therapeutic use include hypersensitivity reactions, nausea, weakness, skin rash, weight loss inflammation of the mouth (stomatitis), itching sensation (pruritus), decreased white blood cells (leukopenia), decreased red blood cell count (anemia), lung inflammation (pneumonitis), and infection.

Acute Toxicity: (Species, Route, End Point, Dose)

Temsirolimus
Rat Oral Minimum Lethal Dose > 100 mg/kg
Rat IV LD 50 50mg/kg
Mouse Oral Minimum Lethal Dose > 100mg/kg
Mouse Intravenous LD 50 > 50mg/kg

Citric acid, anhydrous
Rat Oral LD50 3000 mg/kg

Ethanol
Mouse Oral LD50 3,450 g/m^3
Rat Oral LD50 7,060mg/kg
Mouse Inhalation LC50 4h 39g/m^3
Rat Inhalation LC50 10h 20,000ppm

Propylene glycol
Rat Oral LD 50 22,000 mg/kg
Mouse Oral LD 50 24,900mg/kg
Rabbit Dermal LD 50 20,800mg/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Citric acid, anhydrous
Eye Irritation Rabbit Severe
Skin Irritation Rabbit Mild

Ethanol
Eye Irritation Rabbit Severe

Propylene glycol
Skin Irritation Rabbit Mild
Eye Irritation Rabbit Mild

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Temsirolimus
2 Week(s) Mouse Oral 10 mg/kg/day LOAEL Male reproductive system

11. TOXICOLOGICAL INFORMATION

3 Month(s)	Mouse	Oral	10 mg/kg/day	LOAEL	Skin
1 Month(s)	Rat	Oral	5 mg/kg/day	LOAEL	Lymphoid tissue, Blood
3 Month(s)	Rat	Oral	0.5 mg/kg/day	LOAEL	Pancreas, Eyes
6 Month(s)	Rat	Oral	0.3 mg/kg/day	NOAEL	None identified
1 Month(s)	Non-human Primate	Oral	0.7 mg/kg/day	LOAEL	Gastrointestinal system
3 Month(s)	Non-human Primate	Oral	>= 0.1 mg/kg/day	LOAEL	Gastrointestinal system
9 Month(s)	Non-human Primate	Oral	0.06 mg/kg/day	NOAEL	None identified

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Temsirolimus

Fertility & Early Embryonic Development - Males	Rat	Oral	0.5 mg/kg/day	LOAEL	Fertility
Fertility & Early Embryonic Development-Females	Rabbit	Oral	1 mg/kg/day	NOAEL	Fertility, Reproductive toxicity
Fertility & Early Embryonic Development-Females	Rat	Oral	1 mg/kg/day	LOAEL	Developmental toxicity
Embryo / Fetal Development	Rat	Oral	0.45 mg/kg/day	NOAEL	Maternal Toxicity
Embryo / Fetal Development	Rat	Oral	0.45 mg/kg/day	LOAEL	Fetotoxicity
Embryo / Fetal Development	Rabbit	Oral	0.60 mg/kg/day	LOAEL	Maternal Toxicity, Fetotoxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Temsirolimus

Bacterial Mutagenicity (Ames)	*Salmonella* , *E. coli*	Negative
Mammalian Cell Mutagenicity	Mouse Lymphoma	Negative
Chromosome Aberration	Chinese Hamster Ovary (CHO) cells	Negative
In Vivo Micronucleus	Mouse Bone Marrow	Negative

Carcinogen Status: Carcinogenicity of the mixture has not been determined. Alcohol is listed as a carcinogen by IARC. The IARC monograph examining the carcinogenic potential of ethanol examined only alcoholic beverages.

Ethanol

IARC: Group 1 (Carcinogenic to Humans)

12. ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this mixture have not been fully evaluated. See aquatic toxicity data for individual components below: Releases to the environment should be avoided.

Toxicity:

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Temsirolimus

Pseudokirchneriella subcapitata (Green Alga)	OECD	EbC50	72 Hours	0.063 mg/L
Pimephales promelas (Fathead Minnow)	OECD	LC50	96 Hours	> 4.8 mg/L
Daphnia Magna (Water Flea)	OECD	EC50	48 Hours	> 3.6 mg/L

Ethanol

Fingerling Trout	NPDES	LC50	24 Hours	11,200 mg/L
Oncorhynchus mykiss (Rainbow Trout)	NPDES	LC50	96 Hours	12,900 mg/L
Pimephales promelas (Fathead Minnow)	NPDES	LC50	96 Hours	14,200 mg/L

Bacterial Inhibition: (Inoculum, Method, End Point, Result)

Temsirolimus
Activated sludge OECD EC50 > 1 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential:
Partition Coefficient: (Method, pH, Endpoint, Value)
Temsirolimus
Measured 6.75 Log P 4.93

Mobility in Soil: No data available

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

This material is regulated for transportation as a hazardous material/dangerous good.

UN number: UN 1170
UN proper shipping name: Ethanol solution
Transport hazard class(es): 3
Packing group: II

Flash Point (°C): 21.1

Flash Point (°C): 21.1

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

Citric acid, anhydrous

15. REGULATORY INFORMATION

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	201-069-1

DL-Alpha tocopherol

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	233-466-0

Ethanol

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	carcinogen 4/29/2011 in alcoholic beverages developmental toxicity 10/1/1987 in alcoholic beverages
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	200-578-6

Temsirolimus

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	Not Listed

Propylene glycol

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	200-338-0

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Reproductive toxicity-Cat.1B; H360FD - May damage fertility. May damage the unborn child.
Flammable liquids-Cat.2; H225 - Highly flammable liquid and vapor
Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life
Hazardous to the aquatic environment, chronic toxicity-Cat.1; H410 - Very toxic to aquatic life with long lasting effects

Data Sources:	Pfizer proprietary drug development information. Publicly available toxicity information. Safety data sheets for individual ingredients.
Reasons for Revision:	Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 3 - Composition / Information on Ingredients.
Revision date:	30-Jan-2019

Product Stewardship Hazard Communication
Prepared by: Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet